



CUL3 gene

cullin 3

Normal Function

The *CUL3* gene provides instructions for making a protein called cullin-3. This protein plays a role in the cell machinery that breaks down (degrades) unwanted proteins, called the ubiquitin-proteasome system.

Cullin-3 is a core piece of a complex known as an E3 ubiquitin ligase. E3 ubiquitin ligases function as part of the ubiquitin-proteasome system by tagging damaged and excess proteins with molecules called ubiquitin. Ubiquitin serves as a signal to specialized cell structures known as proteasomes, which attach (bind) to the tagged proteins and degrade them. The ubiquitin-proteasome system acts as the cell's quality control system by disposing of damaged, misshapen, and excess proteins. This system also regulates the level of proteins involved in several critical cell activities such as the timing of cell division and growth.

E3 ubiquitin ligases containing the cullin-3 protein tag proteins called WNK1 and WNK4 with ubiquitin. These proteins are involved in controlling blood pressure in the body. By regulating the amount of WNK1 and WNK4 available, cullin-3 plays a role in blood pressure control.

Health Conditions Related to Genetic Changes

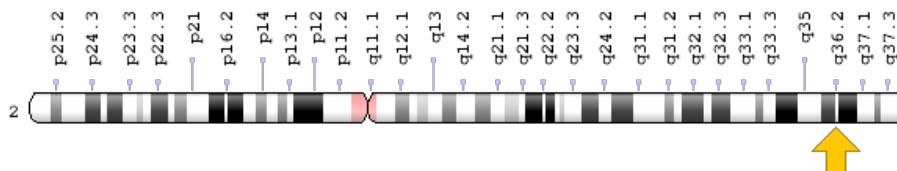
pseudohypoaldosteronism type 2

At least 17 mutations in the *CUL3* gene can cause pseudohypoaldosteronism type 2 (PHA2), a condition characterized by high blood pressure (hypertension) and high levels of potassium in the blood (hyperkalemia). These mutations lead to production of an abnormally short cullin-3 protein that is missing a region. Studies show that this change alters the function of the E3 ubiquitin ligase complex. The change leads to impaired degradation of the WNK4 protein, although the exact mechanism is unclear. The resulting excess of WNK4 protein disrupts normal control of blood pressure, causing hypertension and other features of PHA2. It is unknown if WNK1 is affected by the alterations to the E3 ubiquitin ligase or whether WNK1 plays a role in PHA2 caused by *CUL3* gene mutations.

Chromosomal Location

Cytogenetic Location: 2q36.2, which is the long (q) arm of chromosome 2 at position 36.2

Molecular Location: base pairs 224,470,150 to 224,585,397 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CUL-3
- cullin-3 isoform 1
- cullin-3 isoform 2
- cullin-3 isoform 3
- PHA2E

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Protein Turnover is Tightly Regulated
<https://www.ncbi.nlm.nih.gov/books/NBK22397/>

GeneReviews

- Pseudohypoaldosteronism Type II
<https://www.ncbi.nlm.nih.gov/books/NBK65707>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28CUL3%5BTIAB%5D%29+OR+%28cullin+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D>

OMIM

- CULLIN 3
<http://omim.org/entry/603136>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_CUL3.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=CUL3%5Bgene%5D>
- HGNC Gene Family: Cullins
<http://www.genenames.org/cgi-bin/genefamilies/set/1032>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=2553
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/8452>
- UniProt
<http://www.uniprot.org/uniprot/Q13618>

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Reviewed: March 2016
Published: March 21, 2017

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